



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,813	10/06/2003	Stephen R. Jaspers	02-23	7793
7590 03/07/2007				
Christine Bellas Amgen 1201 Amgen Court West Seattle, WA 98119-3105		EXAMINER SZPERKA, MICHAEL EDWARD		
		ART UNIT 1644		
PAPER NUMBER				
SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE		
3 MONTHS	03/07/2007	PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/679,813	Applicant(s) JASPERS ET AL.	
	Examiner Michael Szperka	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 December 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) ☒ Notice of References Cited (PTO-892) | 4) ☐ Interview Summary (PTO-413) |
| 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) ☐ Information Disclosure Statement(s) (PTO/SB/08) | 5) ☐ Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) ☐ Other: _____ |

DETAILED ACTION

1. Applicant's response and amendment received December 21, 2006 is acknowledged.

Claims 1-25 are pending in the instant application.

Applicant's election with traverse of Group III in the reply filed on December 21, 2006 is acknowledged. The traversal is on the grounds that there is no search burden in concurrently examining all pending claims. In view of the prior art and applicant's persuasive arguments, the restriction requirement has been withdrawn.

Claims 1-25 are under examination as they read on methods of forming peptide antibody complexes.

Claim Objections

2. Claim 7 is objected to in the recitation of "GHS-R". GHS-R is an abbreviation that stands for growth hormone secretagogue receptor, as evidenced by Howard et al., Feighner et al., and the instant specification (lines 8-27 of page 9 and lines 9-16 of page 11). Note that Howard et al. and Feighner et al. are both cited in the aforementioned passages of the specification. The specification also discloses that the polypeptide sequence of GHS-R is SEQ ID NO:5 (see particularly lines 25-26 of page 9). In the interest of clarity, it is suggested that all abbreviations be spelled out in full upon their first recitation in the independent claim or the first dependent claim wherein the abbreviation is recited. Alternatively, applicant may wish to recite the appropriate SEQ ID number in place of "GHS-R".

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

Art Unit: 1644

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are how signal transduction is inhibited in the provided cell expressing GHS-R.

Specifically, the claim recites providing a GHS-R expressing cell, providing a peptide, and contacting the peptide with an antibody that binds said peptide. The specification discloses that GHS-R is a receptor, that the polypeptide consisting of residues 24-37 of SEQ ID NO:2 is a ligand for GHS-R, and that antibodies can be made that bind said polypeptide and antagonize the binding of said polypeptide to said receptor. The polypeptide of SEQ ID NO:2 is not membrane bound, and as such the binding interaction between the polypeptide and antibody occurs in solution. Note that the recited steps of providing do not indicate that the cell and polypeptide are mixed together such that any interaction is possible. Further, even if the cells and polypeptides were mixed together, the presence of the antibody bound to the peptide would preclude any interaction. Therefore, the recited method steps do not physically do anything to the cell since the antibody effectively removes the polypeptide from any potential reaction mixture. As such, nothing has happened to change the cell itself such that signal transduction is inhibited, and the recited method is equivalent to providing a cell isolated from its environment. An environmentally isolated cell would be perfectly competent to transduce a signal via a receptor but would not display signal transduction because of the lack of an appropriate ligand. Similarly, applicant's recited method does nothing that intrinsically inhibits the ability of the GHS-R expressing cell to transduce a signal.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

Art Unit: 1644

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-7 and 17-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Sheppard et al., (WO 01/38355, see entire document).

Sheppard et al. teach the human zsig33 polypeptide and antibodies that bind this polypeptide (see entire document, particularly the abstract). This polypeptide is identical to SEQ ID NO:2 of the instant invention. Suitable epitopes for making antibodies that bind zsig33 are disclosed as comprising residues 24-37 of SEQ ID NO:2, and a working example is disclosed wherein antibodies which specifically recognize the peptide consisting of SEQ ID NO:16 were made (see particularly lines 8-20 of page 34, Example 8 on page 80, and note that SEQ ID NO:16 comprises residues 24-37 of SEQ ID NO:2). Note that the disclosed methods of making antibodies include in vitro exposure of lymphocytes to zsig33 as well as selection via antibody surface display libraries in phage and bacteria (see particularly from line 8 of page 36 to line 15 of page 38). The antibodies of Sheppard are taught as occurring many forms including humanized antibodies that are preferred for administration to humans due to their increased half-life and decreased immunogenicity (see particularly the paragraph spanning pages 35 and 36).

The antibodies of Sheppard et al. are taught for use in many methods. One method is purifying zsig33 polypeptides (see particularly lines 23-30 of page 37). Other methods include in vivo diagnostic and therapeutic applications wherein an anti-zig33 antibody is administered to a mammal (see particularly lines 8-15 of page 38). Anti-zsig33 antibodies are taught as being neutralizing antibodies or antagonists that block the binding of zsig33 to GHS-R in vitro and in vivo (see particularly lines 23-30 of page 37). Sheppard et al. further disclose that antagonists block zsig33 binding and signal transduction in vitro and in vivo, and that secretion of growth hormone can be regulated by the formation of a peptide receptor complex between zsig33 and GHS-R (see particularly lines 3-7 of page 37 and lines 19-20 of page 11). The portion of SEQ ID NO:2 that is responsible for binding to GHS-R is disclosed as being residues 24-37 of SEQ ID NO:2 (see example 9). Growth hormone secretagogues (GHS) stimulate the

Art Unit: 1644

release of growth hormone when they bind the GHS-R receptor present in the pituitary and hypothalamus, and zsig33 is disclosed as being a growth hormone secretagogue (see particularly lines 14-20 of page 11 and lines 22-24 of page 54). As such, antagonizing the interaction between zsig33 and GHS-R, such as by formation of an antibody/polypeptide complex, leads to decreased growth hormone secretion. Also note that anytime an anti-zsig33 antibody binds zsig33, a peptide-antibody complex has been formed.

Therefore, the prior art anticipates the claimed invention.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 8-16 and 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sheppard et al., (WO 01/38355, see entire document) in view of Bednarek (WO 01/92292, see entire document) as evidenced by the Merck Manual of Diagnosis and Therapy.

The teachings of Sheppard et al. have been discussed above. These teachings differ from the claimed invention in that while Sheppard et al. teach methods of administering antagonists, such as antibodies that bind a polypeptide comprising residues 24-37 of SEQ ID NO:2, to patients to inhibit signal transduction and growth

Art Unit: 1644

hormone secretion, they do not teach that administering said antibodies reduces weight, decreases fat deposition, suppresses appetite, or treats metabolic disorders in patients. As such, Sheppard et al. do not teach the selective administration of their antibodies to patients that are in need of reduced weight, decreased fat deposition, suppressed appetite, or metabolic disorder treatment.

Bednarek teaches that ghrelin antagonists are to be administered to humans to facilitate weight loss, decrease appetite, facilitate weight maintenance, treat obesity, and treat diabetes (see entire document, particularly lines 7-15 of page 6). The polypeptide of SEQ IDS NO:2 of the instant invention, also disclosed as zsig33 by the instant invention, is human ghrelin (see enclosed sequence alignment).

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the antibody antagonists disclosed by Sheppard et al. in the methods disclosed by Bednarek. Motivation to do so comes from the teachings of Bednarek that administration of antagonists provides the advantages of treating various human disorders such as obesity and diabetes and from the teachings of Sheppard et al. that their antagonist antibodies are suitable for in vivo use, with humanized antibodies offering the particular advantages of increased half-life and decreased immunogenicity when administered to humans. Therefore, a skilled artisan would realize that he could effectively treat human diseases such as obesity and diabetes by administering the antagonist antibodies of Sheppard et al.

Note that the Merck Manual defines obesity as the excessive accumulation of body fat, and therefore a method of treating obesity would necessarily decrease body fat (see entire document, particularly page 58). Note also that diabetes is a metabolic disorder of glucose metabolism (Ibid, see particularly pages 165-177).

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims

Art Unit: 1644

are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 1-3 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 11 of copending Application No. 10/927,484. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending claims anticipate the instant claims.

Specifically, claim 11 of the '484 application recites "A method for reducing the activity of a polypeptide comprising administering an antibody that specifically binds to the polypeptide, wherein the polypeptide comprises an amino acid sequence of SEQ ID NO: 2 from amino acid 24 to amino acid 37." When the antibody binds the recited polypeptide a complex is necessarily formed. The copending claim recites that the formation of the antibody/polypeptide complex "reduces the activity of the polypeptide" whereas the instant claims do not require the complex to comprise any functional activity or significance, thus making the instant claims broader in scope. Note that SEQ ID NO:2 is identical in both applications. Therefore, the copending claim anticipates the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. Claims 5-7 and 17-19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 11 of copending Application No. 10/927,484 in view of Sheppard et al (WO 01/38355).

The copending claim recites administering an antibody that reduces the activity of a polypeptide comprising residues 24-37 of SEQ ID NO:2, but the activity of said polypeptide is not recited.

Sheppard et al. teach that SEQ ID NO:2 is a growth hormone secretagogue (GHS) that causes the release of growth hormone from pituitary cells when SEQ ID NO:2 binds its receptor, GHS-R, and teach that antibodies can be administered to patients to antagonize this interaction (see entire document, particularly lines 14-20 of page 11, page 37, and lines 22-24 of page 54). Such antibodies when humanized offer the advantages of increased half-life and decreased immunogenicity (see particularly the paragraph spanning pages 35 and 36). Sheppard et al. also disclose an antibody that binds a peptide consisting of SEQ ID NO:16, and that their antibodies can be used in methods of purifying polypeptides.

Therefore, a skilled artisan would know that antibodies that reduce the activity of SEQ ID NO:2 can be administered to humans to reduce growth hormone secretion, and that this reduction in secretion occurs because an antibody/polypeptide complex is formed that prevents the association of SEQ ID NO:2 with its receptor GHS-R. A skilled artisan would also know that such antibodies could be used to purify polypeptides, and that affinity purification relies upon the formation of an antibody/polypeptide complex as a selection mechanism to increase purity of the polypeptide.

This is a provisional obviousness-type double patenting rejection.

12. Claims 8-16 and 20-25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 11 of copending Application No. 10/927,484 in view of Sheppard et al (WO 01/38355) as applied to claims 5-7 and 17-19 above, and further in view of Bednarek (WO 01/92292, see entire document) as evidenced by the Merck Manual of Diagnosis and Therapy.

The teachings of the copending claim and the art of Sheppard et al. have been discussed above. These teachings differ from the claimed invention in that they do not indicate that the antibodies which decrease the activity of a polypeptide comprising amino acids 24-37 of SEQ ID NO:2 should be administered to patients in need to weight loss, decreased fat deposition, appetite suppression, or metabolic disorders.

The copending claim recites administering an antibody that reduces the activity of a polypeptide comprising residues 24-37 of SEQ ID NO:2, but the activity of said polypeptide is not recited.

Bednarek teaches that ghrelin antagonists are to be administered to humans to facilitate weight loss, decrease appetite, facilitate weight maintenance, treat obesity, and treat diabetes (see entire document, particularly lines 7-15 of page 6). The polypeptide of SEQ IDS NO:2 of the instant invention, also disclosed as zsig33 by the instant invention, is human ghrelin (see enclosed sequence alignment).

Note that the Merck Manual defines obesity as the excessive accumulation of body fat, and therefore a method of treating obesity would necessarily decrease body fat (see entire document, particularly page 58). Note also that diabetes is a metabolic disorder of glucose metabolism (Ibid, see particularly pages 165-177).

Therefore, a person of ordinary skill in the art at the time the invention was made would have been motivated to use above discussed antibody antagonists in the methods disclosed by Bednarek so that important human conditions such as diabetes could be treated with an agent that offers the advantages of increased half-life and decreased immunogenicity when administered to humans.

This is a provisional obviousness-type double patenting rejection.

13. No claims are allowable.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8:00-4:30.

Art Unit: 1644

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

A handwritten signature in black ink, appearing to read "Michael Szperka", with a long horizontal flourish extending to the right.

Michael Szperka, Ph.D.
Patent Examiner
Technology Center 1600
March 3, 2007